

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Mohamed Attawia, Hassan Serhan, Thomas M. DiMauro, Melissa Grace and David Urbahns

For: AUTOLOGOUS TREATMENT OF DEGENERATED DISC WITH CELLS

Date: 11/13/03

EXPRESS MAIL LABEL NO. EV 052029486 US

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This Information Disclosure Statement is submitted:

☐ under 37 CFR 1.129(a), or  
(First/Second submission after Final Rejection)

☒ under 37 CFR 1.97(b), or  
(Within any one of the following time periods: three months of filing national application (other than a CPA) or date of entry of the national stage in an international application; or before the mailing date of a first office action on the merits in a non-provisional application, including a CPA, or a Request for Continued Examination).

☐ under 37 CFR 1.97(c) together with either:

☐ a Statement under 37 CFR 1.97(e), as checked below, or

☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(After the 37 CFR 1.97(b) time period, but before final action or notice of allowance, whichever occurs first)

☐ under 37 CFR 1.97(d) together with:

☐ a Statement under 37 CFR 1.97(e), as checked below, and

☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(Filed after final action or notice of allowance, whichever occurs first, but on or before payment of the issue fee)

☐ under 37 CFR 1.97(i):

Applicant requests that the IDS and cited reference(s) be placed in the application filewrapper.  
(Filed after payment of issue fee)

Statement Under 37 CFR 1.97(e)

- ☐ Each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement; or
- ☐ No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

Statement Under 37 CFR 1.704(d) (Patent Term Adjustment)

Applies to original applications (other than design) filed on or after May 29, 2000

- ☐ Each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.
- ☒ Enclosed herewith is form PTO-1449:
  - ☒ Copies of the cited references are enclosed.
  - ☒ Since this application was filed after June 30, 2003, copies of issued U.S. patents and published U.S. applications are not required and are not being provided.
  - ☐ Copies of the cited references are enclosed except those entered in prior application, U.S. Application No. [ ], to which priority under 35 U.S.C. 120 is claimed. [The earlier application contains copies of the cited references.]
  - ☐ The listed references were cited in the enclosed International Search Report in a counterpart foreign application.
  - ☐ The "concise explanation" requirement (non-English references) for reference(s) [ ] under 37 CFR 1.98(a)(3) is satisfied by:
    - ☐ the explanation provided on the attached sheet.
    - ☐ the explanation provided in the Specification.
    - ☐ submission of the enclosed International Search Report.
    - ☐ submission of the enclosed English-language version of a foreign Search Report and/or foreign Office Action.
    - ☐ the enclosed English language abstract.

☐ Applicant requests that the following non-published pending applications be considered:

Examiner's  
Initials

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_  
Examiner

\_\_\_\_\_  
Date

☐ A copy of each above-cited application, including the current claims, is enclosed.

☐ A copy of each above-cited application, including the current claims, is enclosed, except those entered in prior application, U.S. Application No. [ ], to which priority under 35 U.S.C. 120 is claimed.

The Examiner is requested to return a copy of the above list of pending applications indicating which references were considered with the next office communication.

It is requested that the information disclosed herein be made of record in this application.

Method of payment:

☐ A check for the fee noted above is enclosed, or the fee has been included in the check with the accompanying Reply. A copy of this Statement is enclosed.

☐ Please charge Deposit Account 08-0380 in the amount of \$[ ]. A copy of this Statement is enclosed.

☒ Please charge any deficiency in fees and credit any overpayment to Deposit Account 08-0380.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

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Dated: November 13, 2003

PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>November 13, 2003</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3518.1012-004		APPLICATION NO.	
	APPLICANTS Mohamed Attawia <i>et al.</i>			
	FILING DATE November 13, 2003		CONFIRMATION NO.	GROUP

U.S. PATENT DOCUMENTS				
EXAM- INER INI- TIAL	REF. NO.	DOCUMENT NUMBER	ISSUE DATE / PUBLICATION DATE	NAME
	AA	6,340,369 B1	01/22/02	Ferree
	AB	6,352,557 B1	03/05/02	Ferree
	AC	2003/0069639 A1	04/10/03	Sander <i>et al.</i>

		OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
	AR	Alini, M., <i>et al.</i> , "A Biological Approach to Treating Disc Degeneration: Not for Today, but Maybe for Tomorrow," <i>Eur. Spine J.</i> , 11 (Suppl. 2): S215-S220 (2002).
	AS	Connolly, J., <i>et al.</i> , "Development of an Osteogenic Bone-Marrow Preparation," <i>The Journal of Bone and Joint Surgery, Inc.</i> , 71-A (5): 684-691 (1989).
	AT	Ganey, T. M. and Meisel, H. J., "A Potential Role for Cell-Based Therapeutics in the Treatment of Intervertebral Disc Herniation," <i>Eur. Spine J.</i> , 11 (Suppl. 2): S206-S214 (2002).
	AU	Sakai, D., <i>et al.</i> , "Transplantation of Mesenchymal Stem Cells Embedded in Atelocollagen® Gel to the Intervertebral Disc: A Potential Therapeutic Model for Disc Degeneration," <i>Biomaterials</i> , 24: 3531-3541 (2003).
	AV	Ohtori, S., <i>et al.</i> , "TNF- $\alpha$ and TNF- $\alpha$ Receptor 1 Upregulation in GLIA and Neurons After Nerve Injury. Studies in Murine DRG and Spinal Cord," 13, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
	AW	Korhonen, T., <i>et al.</i> , "Efficacy of Infliximab for Disc Herniation-Induced Sciatica One-Year Follow-Up," 14, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
	AX	Sakai, D., <i>et al.</i> , "Autologous Transplantation of Mesenchymal Stem Cells for Disc Repair," 24, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
	AY	Le Visage, C., <i>et al.</i> , "Interaction of Human Mesenchymal Stem Cells with Disc Cells: Changes in Biosynthesis of Extracellular Matrix," 25, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).

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AZ	Risbud, M. V., <i>et al.</i> , "Mesenchymal Stem Cells Respond to Their Microenvironment <i>In Vitro</i> to Assume Nucleus Pulposus-Like Phenotype," 26, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AR2	Richardson, S., <i>et al.</i> , "Human Bone Marrow Mesenchymal Stromal Cells as a Source of Chondrocytes for Treatment of Intervertebral Disc Degeneration," 27, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AS2	Ahn, N. U., <i>et al.</i> , "Effect of Nutrient Concentration and OP-1 on the Metabolism of Intervertebral Disc: <i>In Vitro</i> Organ Culture Study," 28, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AT2	Kwon, U-H., <i>et al.</i> , "Dexamethsone Stimulates Cellular Proliferation While Downregulates Matrix Synthesis in Intervertebral Disc Cells," 29, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AU2	Li, J., <i>et al.</i> , "The Effects of Bone Morphogenetic Protein 2 (BMP-2) and Cartilage-Derived Morphogenetic Protein 2 (CDMP-2) on Aggrecan Gene Expression in Chondrocytes," 30, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AV2	Yoon, S. T., <i>et al.</i> , "LMP-1 Upregulates Proteoglycan Synthesis in Intervertebral Disc Cells Through a BMP Mediated Process," 31, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AW2	Cornefjord, M., <i>et al.</i> , "Cerebrospinal Fluid Biomarkers in Experimental Spinal Nerve Root Injury," 38, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AX2	Takada, T., <i>et al.</i> , "IL-6 Production was Upregulated by Interaction Between Disc Tissue and Macrophages," 41, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AY2	Inui, Y., <i>et al.</i> , "Fas-Ligand Expression on Nucleus Pulposus Cells Begins in Developing Embryo," 42, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AZ2	Sobajima, S., <i>et al.</i> , "Stem Cell Therapy for Degenerative Disc Disease: An In-Vitro Feasibility Study," 43, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).

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	FILING DATE <b>November 13, 2003</b>	CONFIRMATION NO.	GROUP

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

AR3	Imai, Y., <i>et al.</i> , "The Quantification of Cytokine-Induced Matrix Catabolism in Tissue Engineered Intervertebral Discs," 67, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AS3	Hunter, C. J., <i>et al.</i> , "Functional Behavior of Notochordal Cell Clusters in the Canine Nucleus Pulposus: Cell Communication and Survival," 70, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AT3	Tsuji, T., <i>et al.</i> , "Age-Related Changes in M-RNA Expression of Various Regulatory Factors in Rabbit Intervertebral Disc," 81, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AU3	Miyamoto, H., <i>et al.</i> , "The Effect of Mechanical Stress on the Production of Inflammatory Agents by Disc Cells," 110, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AV3	Arai, I., <i>et al.</i> , "Pretreatment with Loxoprofen Sodium, 6-OHDA or Anti TNF-Alpha Antibody Reduce Fos-Like Immunoreactivity in Rat Experimental Lumbar Disc Herniation," 111, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AW3	Edwards, S. L., <i>et al.</i> , "Radiographic Assessment of Posterolateral Spine Fusion With and Without Platelet Rich Plasma," 117, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AX3	Xie, X., <i>et al.</i> , "Treatment of Spondylodiscitis Intravenous Versus Percutaneous Intradiscal Applications of Antibiotics: An Experimental Study in Rabbits," 120, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AY3	Frain, J., <i>et al.</i> , "Use of cDNA Microarrays to Investigate Cytokine Expression in Intervertebral Disc Degeneration," 126, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AZ3	Hashizume, H., <i>et al.</i> , "Role of IL-8, MCP-1 and PH in Neuropathic Pain Enhanced by Degenerative Nucleus Pulposus," 127, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AR4	Lotz, J. C., <i>et al.</i> , "Cytokines in Normal, Degenerated, and Nucleoplasty-Treated Porcine Discs," 157, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).

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**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

AS4	Okuma, M., <i>et al.</i> , "Rotary Cell Culture System Stimulates Annulus Fibrosus Cell Proliferation but Suppresses Proteoglycan Metabolism," 164, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AT4	Burke, J. G., <i>et al.</i> , "Human Nucleus Pulposus Secretes Transforming Growth Factor Beta-1 and Basic Fibroblast Growth Factor," 189, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AU4	Kato, H., <i>et al.</i> , "The Effect of IL-1 on the Rabbit Intervertebral Disc In Vivo," 199, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AV4	Imai, Y., <i>et al.</i> , "Effect of Recombinant Human Osteogenic Protein-1 on Extracellular Matrix Metabolism by Human Annulus Fibrosus and Nucleus Pulposus Cells," 205, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AW4	Lee, C. S., <i>et al.</i> , "A Single Period of Hyperphysiologic Stretch Induces IL-6, TGF-beta and Cell Proliferation in Anulus Fibrosus Cells," 215, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AX4	Le Maitre, C. L., <i>et al.</i> , "Response of Human Intervertebral Disc Cells to IL-1," 216, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AV4	Le Maitre, C. L., <i>et al.</i> , "Expression of the IL-1 Family in Human Intervertebral Disc," 217, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AZ4	Weiler, C., <i>et al.</i> , "Expression of TNF- $\alpha$ in Autopsy and Biopsy Specimens of Intervertebral Discs of Various Age and Degeneration," 233, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AR5	Ohtori, S., <i>et al.</i> , "TNF- $\alpha$ -Deficient Mice Have Fewer Macrophages in Injured Nerve and Reduced Glial Activation in DRG and Spinal Cord," 250, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).
AS5	Igarashi, A., <i>et al.</i> , "Inflammatory Cytokines Release From Facet Joint Tissue in Degenerative Lumbar Disorders," 262, <i>Abstracts of the 30<sup>th</sup> Annual Meeting of the International Society for the Study of the Lumbar Spine</i> , Vancouver, Canada (May 2003).

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